General

Guideline Title

Guideline for the management of bleeding on Dabigatran (Pradaxa).

Bibliographic Source(s)

Guideline for the management of bleeding on dabigatran (Pradaxa). Portland (ME): Maine Medical Center, Department of Emergency Medicine; 2012 Feb 9. 3 p. [10 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Levels of evidence grading (A, B, C, D, M, R and X) are defined at the end of the "Major Recommendations" field.

General Care for All Patients

- Hold dabigatran (van Ryn et al., 2010; Hankey & Eikelboom, 2011) [R]
- Obtain laboratory studies including complete blood count (CBC), activated partial thromboplastin time (aPTT), creatinine, liver function tests (LFTs), international normalized ratio (INR), thrombin clotting time, fibrinogen activity (van Ryn et al., 2010; Hankey & Eikelboom, 2011; Institute for Clinical Systems Improvement [ICSI], "Dabigatran," 2011) [R]
- Evaluate for anatomic defects explaining hemorrhage (van Ryn et al., 2010; Hankey & Eikelboom, 2011) [R]
- Use local measures to control bleeding (van Ryn et al., 2010; Hankey & Eikelboom, 2011) [R]
- Consider the need for surgical intervention, embolization to control bleeding (van Ryn, et al., 2010; Hankey & Eikelboom, 2011) [R]
- Consider the need for Hematology/Nephrology consults (van Ryn et al., 2010; Hankey & Eikelboom, 2011) [R]

For Patients with Mild Bleeding

- Continue "General Care for All Patients" listed above, and:
- Delay next dabigatran dose (van Ryn et al., 2010; Hankey & Eikelboom, 2011) [R]
- Discontinue dabigatran treatment if appropriate (van Ryn et al., 2010; Hankey & Eikelboom, 2011) [R]
- Supportive care/symptomatic treatment (van Ryn et al., 2010; Hankey & Eikelboom, 2011) [R]

For Patients with Moderate to Severe Bleeding

- Discontinue dabigatran (van Ryn et al., 2010; Hankey & Eikelboom, 2011) [R]

- Supportive care/symptomatic treatment (van Ryn et al., 2010; Hankey & Eikelboom, 2011) [R]
- Activated charcoal at standard doses if last dose of dabigatran etexilate within 2 hours (van Ryn et al., 2010; Hankey & Eikelboom, 2010; van Ryn et al., 2009) [R]
- Maintain adequate diuresis with fluid replacement and hemodynamic support as needed (van Ryn et al., 2010; Hankey & Eikelboom, 2011; van Ryn et al., 2009; Stangier, 2008; Stangier et al., 2010) [B]
- Transfuse red blood cells (RBCs) as needed to maintain hemoglobin (HgB) above 8 gm/dL (Hankey & Eikelboom, 2011; ICSI, "Antithrombotic," 2011) [R]
- If more than 4 units of RBCs are required, transfuse RBCs/plasma 1:1 to avoid a dilutional coagulopathy (Stangier et al., 2008) [B]
- See also Maine Medical Center *Massive Transfusion Protocol*.
- Consultation with nephrology for consideration of dialysis (van Ryn et al., 2010; Stangier et al., 2010; Stangier et al., 2008) [B]

For Patients with Severe/Life Threatening Bleeding

- Continue "General Care," and "Moderate to Severe Bleeding" measures above, and:
- Consider recombinant activated Factor VII (40 mcg/kg) or (van Ryn et al., 2008; Eerenberg et al., 2011) [R]
- As a last resort, consider prothrombin complex concentrate (PCC) (25 units/kg) to help with clot formation at the site of bleeding (van Ryn et al., 2008; Eerenberg et al., 2011) [R]
- NOTE: The strength of the evidence for these interventions is weak and limited.

Definitions:

Evidence Grading

Primary Reports of New Data Collections

A Randomized, controlled trial

B Cohort study

C Non-randomized trial with concurrent or historical controls

- Case-control study
- Study of sensitivity/specificity of a diagnostic test
- Population-based descriptive study

D Cross-sectional study

- Case series
- Case report

Reports That Synthesize or Reflect Upon Collections of Primary Reports

M Meta-analysis

- Systematic review
- Decision analysis
- Cost-effectiveness analysis

R Consensus statement

- Consensus report
- Narrative review

X Medical opinion

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Bleeding induced by the direct thrombin inhibitor dabigatran etexilate (Pradaxa)

Guideline Category

Evaluation

Management

Treatment

Clinical Specialty

Emergency Medicine

Family Practice

Hematology

Internal Medicine

Nephrology

Neurology

Nursing

Pharmacology

Surgery

Intended Users

Advanced Practice Nurses

Nurses

Pharmacists

Physical Therapists

Physician Assistants

Guideline Objective(s)

To present a clinical guideline for the evaluation and management of patients who present to the emergency department with bleeding induced by the direct thrombin inhibitor dabigatran etexilate (Pradaxa)

Target Population

Any patient receiving oral anticoagulation with the therapeutic agent dabigatran etexilate (Pradaxa)

Interventions and Practices Considered

1. Holding/discontinuing dabigatran
2. Laboratory testing, including complete blood count (CBC), activated partial thromboplastin time (aPTT), creatinine, liver function tests (LFTs), international normalized ratio (INR), thrombin clotting time, and fibrinogen activity
3. Evaluation for anatomical defects explaining hemorrhage
4. Local measures to control bleeding
5. Supportive care/symptomatic treatment
6. Administration of activated charcoal
7. Fluid replacement and hemodynamic support
8. Administration of blood products including packed red blood cells and fresh frozen plasma
9. Consultation with hematology/nephrology specialists as necessary
10. Administration of recombinant activated factor VII
11. Administration of prothrombin complex concentrate
12. Consider need for surgical intervention or embolization
13. Hemodialysis

Major Outcomes Considered

- Risks associated with uncontrolled bleeding
- Risks associated with hemodialysis
- Risks associated with blood product administration

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The MEDLINE and CINAHL databases and the Cochrane Library were used to conduct a literature search to locate relevant articles. The National Guideline Clearinghouse was searched for relevant guidelines. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research although review articles, case reports, and commentaries were also reviewed. Hand searches of relevant journals were conducted to locate relevant articles. Hand searches of the references of relevant articles were conducted to locate related articles.

Timeframes searched:

- Medline (via Ovid): 1946 to September Week 2, 2011
- CINAHL: 2004 to 2011
- Cochrane Database of Systematic Reviews: 2005 to Sept 2011

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Primary Reports of New Data Collections

A Randomized, controlled trial

B Cohort study

C Non-randomized trial with concurrent or historical controls:

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X Medical opinion

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

This guideline was developed from a systematic review and synthesis of current evidence regarding the treatment of bleeding associated with dabigatran etexilate (Pradaxa). Research findings and other evidence, such as guidelines, clinical policies, and standards from professional organizations, case reports, and expert opinion were critiqued, analyzed, and used as supporting evidence.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Peer Review

Description of Method of Guideline Validation

Critical Review Process

This guideline was reviewed by experts knowledgeable regarding research on dabigatran etexilate (Pradaxa) and guideline development.

Approval

This guideline was approved by the Maine Medical Center Department of Emergency Medicine Quality Council, the Maine Medical Center Antithrombotic Task Force, and the Maine Medical Center Pharmacy and Therapeutics Committee.

Evidence Supporting the Recommendations

References Supporting the Recommendations

Eerenberg ES, Kamphuisen PW, Sijpkens MK, Meijers JC, Buller HR, Levi M. Reversal of rivaroxaban and dabigatran by prothrombin complex concentrate: a randomized, placebo-controlled, crossover study in healthy subjects. Circulation. 2011 Oct 4;124(14):1573-9. PubMed

Hankey GJ, Eikelboom JW. Dabigatran etexilate: A new oral thrombin inhibitor. Circulation. 2011 Apr 5;123(13):1436-50. [74 references] PubMed

Institute for Clinical Systems Improvement (ICSI). Antithrombotic therapy supplement. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2011 Apr. 75 p. [175 references]

Institute for Clinical Systems Improvement (ICSI). Dabigatran: consensus-based statement on emergency care of bleeding. [Internet]. Bloomington (MN): Institute for Clinical Systems Improvement; 2011 Sep [accessed 2011 Oct 10].

Stangier J, Rathgen K, Stahle H, Mazur D. Influence of renal impairment on the pharmacokinetics and pharmacodynamics of oral dabigatran etexilate: an open-label, parallel-group, single-centre study. Clin Pharmacokinet. 2010 Apr 1;49(4):259-68. PubMed

Stangier J, Stahle H, Rathgen K, Fuhr R. Pharmacokinetics and pharmacodynamics of the direct oral thrombin inhibitor dabigatran in healthy elderly subjects. Clin Pharmacokinet. 2008;47(1):47-59. PubMed

Stangier J. Clinical pharmacokinetics and pharmacodynamics of the oral direct thrombin inhibitor dabigatran etexilate. Clin Pharmacokinet. 2008;47(5):285-95. PubMed

van Ryn J, Ruehl D, Priepke H, et al. Reversibility of the anticoagulant effect of high doses of the direct thrombin inhibitor daigatran , by recombinant Factor VIIa or activated prothrombin complex concentrate. Haematologia. 2008;93(Suppl 1):148.

van Ryn J, Sieger P, Kink-Eiband M, et al. Adsorption of dabigatran etexilate in water or dabigatran in pooled human plasma by activated charcoal in vitro. In: 51st ASH Annual Meeting and Exposition.Washington (DC): American Society of Hematology; 2009.

van Ryn J, Stangier J, Haertter S, Liesenfeld KH, Wienen W, Feuring M, Clemens A. Dabigatran etexilate - a novel, reversible, oral direct thrombin inhibitor: Interpretation of coagulation assays and reversal of anticoagulant activity. Thromb Haemost. 2010 Mar 29;103(6):1116-27. PubMed

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for selected recommendations (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Minimization the risk of dabigatran-associated morbidity and/or mortality

Potential Harms

- Discomfort and infection risk associated with phlebotomy
- Infection risk and allergic risk associated with blood product administration
- Allergic risk associated with medication administration
- Risks associated with dialysis, including infection, hemodynamic instability, bleeding, electrolyte imbalance, nausea, and anemia

Qualifying Statements

Qualifying Statements

This evidence-based clinical pathway is only a guide. It is highly recommended that all hospital emergency departments develop a plan for the evaluation of patients with bleeding on dabigatran etexilate based upon available resources. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitation unique to the institution or practice setting.

This tool is intended to be a reference for clinicians caring for patients with bleeding while on dabigatran etexilate therapy and is not intended to replace providers' clinical judgment. Some clinical problems may not be adequately addressed by this reference.

Implementation of the Guideline

Description of Implementation Strategy

Description of Implementation Strategy

The guideline developer's implementation strategy includes:

- Educational sessions on clinical pathway implementation
- Distribution of the clinical pathway to all emergency physicians and nurses

- Distribution of the clinical pathway to all hospital clinicians

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Safety

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: This guideline was not adapted from another source.

Date Released

2012 Feb

Guideline Developer(s)

Maine Medical Center, Department of Emergency Medicine - Hospital/Medical Center

Source(s) of Funding

Maine Medical Center, Department of Emergency Medicine

Guideline Committee

Emergency Medicine Quality Council: Bleeding on Dabigatran Work Group

Composition of Group That Authored the Guideline

Work Group Members: Michael R. Baumann, MD, Chair Emergency Medicine; Peter E. Croft, MD, Resident Physician, Emergency Medicine; Tania D. Strout, PhD, RN, MS, Associate Director of Research, Emergency Medicine; Kathryn E. Smith, PharmD, BCPS, Clinical Specialist –

Anticoagulation, Department of Pharmacy

Financial Disclosures/Conflicts of Interest

None stated

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the Maine Medical Center Department of Emergency Medicine Guidelines Web site .

Print copies: Available from Maine Medical Center Department of Emergency Medicine Research Office, 47 Bramhall Street, Portland, ME 04102. Telephone (207) 662-7049. Contact: Tania D. Strout, PhD, RN, MS at strout@mmc.org.

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on July 23, 2012.

Copyright Statement

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Readers with questions regarding guideline content are directed to contact the guideline developer.